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CANCERLIT,
CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
DRUGB,

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=> S PEPTIDE AND BINDING

201	FILE ADISALERTS
93	FILE ADISINSIGHT
1117	FILE AGRICOLA
1669	FILE AIDSLINE
98	FILE ANABSTR
334	FILE AQUASCI
521	FILE BIOBUSINESS
91	FILE BIOCOMMERCE
29833	FILE BIOSIS
1985	FILE BIOTECHABS
1985	FILE BIOTECHDS
1760	FILE CABA
9428	FILE CANCERLIT
41154	FILE CAPLUS
289	FILE CEABA
132	FILE CEN
97	FILE CIN
237	FILE CONFSCI
243	FILE CROPB
56	FILE CROPU
20 FILES SEARCHED...	
806	FILE DDFB
3779	FILE DDFU
31843	FILE DGENE
806	FILE DRUGB
48	FILE DRUGNL
5015	FILE DRUGU
518	FILE EMBAL
31003	FILE EMBASE
46	FILE FROSTI
271	FILE FSTA
2805	FILE GENBANK
5	FILE HEALSAFE
1462	FILE IFIPAT
5571	FILE JICST-EPLUS
36 FILES SEARCHED...	
12	FILE KOSMET
11528	FILE LIFESCI
47522	FILE MEDLINE
48	FILE NIOSHTIC
238	FILE NTIS
42	FILE OCEAN
70	FILE PHAR
2	FILE PHIC
156	FILE PHIN
681	FILE PROMT
29636	FILE SCISEARCH
5708	FILE TOXLINE
10418	FILE TOXLIT
16706	FILE USPATFULL
50 FILES SEARCHED...	
2257	FILE WPIDS
2257	FILE WPINDEX
1	FILE APILIT
17	FILE CBNB
215	FILE COMPENDEX
269	FILE INSPEC

83 FILE INSPHYS
 205 FILE INSTEXT
 42 FILE IIR
 16 FILE KKF
 2 FILE METADEX
 35 FILE NAPRALERT
 4 FILE PAPERCHEM2
 27 FILE RAPRA
 3 FILE RUSSCI

67 FILES SEARCHED...

2 FILE WSCA
 5 FILE COMPUAB
 28 FILE ENERGIE
 2427 FILE ENERGY
 13 FILE FTN
 1076 FILE NLDB
 92 FILE SOLIDSTATE
 24 FILE AEROSPACE
 1 FILE APIPAT

86 FILES SEARCHED...

2470 FILE EUROPATFULL
 1 FILE GEOREF
 1 FILE ISMEC
 286 FILE PATOSEP
 468 FILE PATOSWO
 3 FILE PIRA
 8 FILE POLLUAB
 22 FILE SIGLE

80 FILES HAVE ONE OR MORE ANSWERS, 100 FILES SEARCHED IN STNINDEX

L1 QUE PEPTIDE AND BINDING

=> S PEPTIDE AND BINDING AND NEURAL NET?

1 FILE AIDSLINE
 8 FILE BIOSIS
 9 FILES SEARCHED...
 2 FILE CANCERLIT
 12 FILE CAPLUS
 2 FILE CEN
 1 FILE CIN
 20 FILES SEARCHED...
 1 FILE DDFU
 1 FILE DRUGU
 1 FILE EMBAL
 8 FILE EMBASE
 4 FILE JICST-EPLUS
 36 FILES SEARCHED...
 5 FILE LIFESCI
 13 FILE MEDLINE
 1 FILE PHIN
 45 FILES SEARCHED...
 3 FILE PROMT
 46 FILES SEARCHED...
 14 FILE SCISEARCH
 1 FILE TOXLINE
 45 FILE USPATFULL
 50 FILES SEARCHED...
 1 FILE WPIDS
 1 FILE WPINDEX
 56 FILES SEARCHED...
 58 FILES SEARCHED...

1 FILE INVESTEXT
 59 FILES SEARCHED.
 70 FILES SEARCHED...
 76 FILES SEARCHED...
 2 FILE FTN
 6 FILE NLDB
 81 FILES SEARCHED...
 87 FILES SEARCHED...
 2 FILE EUROPATFULL
 88 FILES SEARCHED...
 1 FILE PATOSWO
 2 FILE SIGLE
 98 FILES SEARCHED...

26 FILES HAVE ONE OR MORE ANSWERS, 100 FILES SEARCHED IN STNINDEX

L2 QUE PEPTIDE AND BINDING AND NEURAL NET?

=> D RANK

F1	45	USPATFULL
F2	14	SCISEARCH
F3	13	MEDLINE
F4	12	CAPLUS
F5	8	BIOSIS
F6	8	EMBASE
F7	6	NLDB
F8	5	LIFESCI
F9	4	JICST-EPLUS
F10	3	PROMT
F11	2	CANCERLIT
F12	2	CEN
F13	2	FTN
F14	2	EUROPATFULL
F15	2	SIGLE
F16	1	AIDSLINE
F17	1	CIN
F18	1	DDFU
F19	1	DRUGU
F20	1	EMBAL
F21	1	PHIN
F22	1	TOXLINE
F23	1	WPIDS
F24	1	WPINDEX
F25	1	INVESTEXT
F26	1	PATOSWO

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=> S PEPTIDE AND BINDING AND NEURAL NET?

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L3 14 PEPTIDE AND BINDING AND NEURAL NET?

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L3 ANSWER 1 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Secondary structure of the C-terminal DNA-binding domain of the transcriptional activator NifA from Klebsiella pneumoniae: Spectroscopic analyses

AU Missaillidis S; Jaseja M; Ray P; Chittock R; Wharton C W; Drake A F; Buck M; Hyde E I (Reprint)

SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (15 JAN 1999) Vol. 361, No. 2, pp. 173-182.
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0003-9861.

AB The conformation of the C-terminal DNA-binding domain of the transcriptional activator NifA from Klebsiella pneumoniae has been probed by circular dichroism (CD), Fourier-transformed infrared (FTIR), and nuclear magnetic resonance (NMR) spectroscopy in combination. Secondary structure prediction suggests that the C-terminal half of the domain contains three alpha-helices. The spectra show that the domain is folded in the absence of DNA and of the N-terminal and central domains of NifA. The three spectroscopic techniques suggest slightly different proportions of secondary structural elements but all suggest that it contains about 33% alpha-helix. These results are in agreement with a previous

prediction

suggesting that NifA contains a helix-turn-helix motif and with the amount

of alpha-helix predicted. The environment of the aromatic residues was examined by CD and NMR spectroscopy, which suggest that one or both of

the

tryptophan residues are involved in the tertiary structure of the protein but that the tyrosine residue in the helix-turn-helix motif is solvent exposed and so available to bind to DNA. The thermal melting profiles and pH-dependent structural changes were also examined by CD spectroscopy. This technique indicates that at low pH there is an increase in the secondary structure and interactions contributing to the tertiary structure. Many of the acidic residues are predicted to be on a single helix, before the helix-turn-helix motif, which may therefore be

important

for maintaining the structure and function of the C-terminal **peptide**; alternatively, the N-terminal half of the domain may become more folded at low pH. (C) 1999 Academic Press.

L3 ANSWER 2 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Predicting peptides that bind to MHC molecules using supervised learning of hidden Markov models

AU Mamitsuka H (Reprint)

SO PROTEINS-STRUCTURE FUNCTION AND GENETICS, (1 DEC 1998) Vol. 33, No. 4, pp. 460-474.

Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK,

NY 10158-0012.
ISSN: 0887-3585.

AB The **binding** of a major histocompatibility complex (MHC) molecule to a **peptide** originating in an antigen is essential to recognizing antigens in immune systems, and it has proved to be important

to use computers to predict the peptides that will bind to an MHC molecule. The purpose of this paper is twofold: First, we propose to apply

supervised learning of hidden Markov models (HMMs) to this problem, which can surpass existing methods for the problem of predicting MHC-binding peptides, Second, we generate peptides that have high probabilities to bind to a certain MRC molecule, based on our proposed method using peptides binding to MHC molecules as a set of training data. From our experiments, in a type of cross-validation test, the discrimination accuracy of our supervised learning method is usually approximately 2-15% better than those of other methods, including backpropagation neural networks, which have been regarded as the most effective approach to this problem. Furthermore, using an HMM trained for HLA-A2, we present new peptide sequences that are provided with high binding probabilities by the HMM and that are thus expected to bind to HLA-A2 proteins. Peptide sequences not shown in this Paper but with rather high binding probabilities-can be obtained from the author (E-mail: mami@ccm.cl.nec.co.jp). (C) 1998 Wiley Liss, Inc.

L3 ANSWER 3 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Enhanced antigenicity of a four-contact-residue epitope of the measles virus hemagglutinin protein by phage display libraries: evidence of a helical structure in the putative active site

AU Deroo S; ElKasmi K C; Fournier P; Theisen D; Brons R H C; Herrmann M; Desmet J; Muller C P (Reprint)

SO MOLECULAR IMMUNOLOGY, (JUN 1998) Vol. 35, No. 8, pp. 435-443.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0161-5890.

AB Antigenicity and conformational propensities of synthetic peptides corresponding to the sequential epitope H236-255 of the measles virus hemagglutinin protein were investigated. This epitope corresponds to the neutralising and protective monoclonal antibody BH129 and includes

Arg243,

implicated in CD46-down-regulation and Arg253 that has been mapped to the putative enzymatic site. Fine mapping with truncation-, elongation-, Gly- and Ala-substitution analogues defined EL-QL as the critical residues of the minimal epitope S(244)ELSQL(249). CD spectra of peptides, comparison with the 3D-structure of homologous sequences, and prediction algorithms suggested a helical structure with the contact residues E245L-QL(249) located on the protein surface. Mimotopes obtained with a 6-mer phage display library contained a consensus Pro (important for binding) instead of Ser,,, of the wild-type sequence (irrelevant for binding). The kink induced by Pro seemed to be essential to bring the 4 contact-residues in the mimotopes and in the corresponding short peptides together. CD analysis and prediction algorithms suggested that non-helical conformations of the phage insert and of the peptides may favourably mimic the antigenic helical turns of the wild-type sequence, resulting in an up to 135 times higher antigenicity of the mAb towards

the

mimotope peptides. (C) 1998 Elsevier Science Ltd. All rights reserved.

L3 ANSWER 4 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Neural network-based prediction of candidate T-cell epitopes

AU Honeyman M C; Brusica V; Stone N L; Harrison L C (Reprint)

SO NATURE BIOTECHNOLOGY, (OCT 1998) Vol. 16, No. 10, pp. 966-969.
Publisher: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707.
ISSN: 1087-0156.

AB Activation of T cells requires recognition by T-cell receptors of specific peptides bound to major histocompatibility complex (MHC)

molecules on the surface of either antigen-presenting or target cells, These peptides, cell epitopes, have potential therapeutic applications, such as for use as vaccines. Their identification, however, usually requires that multiple overlapping synthetic peptides encompassing a protein antigen be assayed, which in humans, is limited by volume of donor blood. T-cell epitopes are a subset of peptides that bind to MHC molecules. We use an artificial **neural network** (ANN) model trained to predict peptides that bind to the MHC class II molecule HLA-DR4(*0401). **Binding** prediction facilitates identification of T-cell epitopes in tyrosine phosphatase IA-2, an autoantigen in DR4-associated type1 diabetes. Synthetic peptides encompassing IA-2 were tested experimentally for DR4 **binding** and T-cell proliferation in humans at risk for diabetes. ANN-based **binding** prediction was sensitive and specific, and reduced the number of peptides required for T-cell assay by more than half, with only a minor loss of epitopes. This strategy could expedite identification of candidate T-cell epitopes in diverse diseases.

L3 ANSWER 5 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI Application of an artificial **neural network** to predict specific class I MHC **binding peptide** sequences
 AU Milik M; Sauer D; Brunmark A P; Yuan L L; Vitiello A; Jackson M R; Peterson P A; Skolnick J; Glass C A (Reprint)
 SO NATURE BIOTECHNOLOGY, (AUG 1998) Vol. 16, No. 8, pp. 753-756.
 Publisher: NATURE PUBLISHING CO, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707.
 ISSN: 1087-0156.

AB Computational methods were used to predict the sequences of peptides that bind to the MHC class I molecule, K-b. The rules for predicting **binding** sequences, which are limited, are based on preferences for certain amino acids in certain positions of the **peptide**. It is apparent though, that **binding** can be influenced by the amino acids in all of the positions of the **peptide**. An artificial **neural network** (ANN) has the ability to simultaneously analyze the influence of all of the amino acids of the **peptide** and thus may improve **binding** predictions. ANNs were compared to statistically analyzed peptides for their abilities to predict the sequences of K-b **binding** peptides. ANN systems were trained on a library of **binding** and nonbinding **peptide** sequences from a phage display library. Statistical and ANN methods identified strong **binding** peptides with preferred amino acids. ANNs detected more subtle **binding** preferences, enabling them to predict medium **binding** peptides. The ability to predict class I MHC molecule **binding** peptides is useful for immunological therapies involving cytotoxic-T cells.

L3 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI Relationship between **peptide** selectivities of human transporters associated with antigen processing and HLA class I molecules
 AU Daniel S; Brusic V; CaillatZucman S; Petrovsky N; Harrison L; Riganelli D;
 Sinigaglia F; Gallazzi F; Hammer J; vanEndert P M (Reprint)
 SO JOURNAL OF IMMUNOLOGY, (15 JUL 1998) Vol. 161, No. 2, pp. 617-624.
 Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
 ISSN: 0022-1767.

AB Efficiency of presentation of a **peptide** epitope by a MHC class I molecule depends on two parameters: its **binding** to the MHC molecule and its generation by intracellular Ag processing. In contrast to the former parameter, the mechanisms underlying **peptide** selection in Ag processing are poorly understood. **Peptide** translocation by the TAP transporter is required for

presentation of most epitopes and may modulate **peptide** supply to MHC class I molecules. To study the role of human TAP for **peptide** presentation by individual HLA class I molecules, we generated artificial **neural networks** capable of predicting the affinity of TAP for random sequence 9-mer peptides. Using **neural network**-based predictions of TAP affinity, we found that peptides eluted from three different HLA class I molecules had higher TAP affinities than control peptides with equal **binding** affinities for the same HLA class I molecules, suggesting that human TAP may contribute to epitope selection. In simulated TAP **binding** experiments with 408 HLA class I **binding** peptides, HLA class I molecules differed significantly with respect to TAP affinities of their ligands. As a result, some class I molecules, especially HLA-B27, may be particularly efficient in presentation of cytosolic peptides with low concentrations, while most class I molecules may predominantly present abundant cytosolic peptides.

L3 ANSWER 7 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Prediction of MHC class II-**binding** peptides using an evolutionary algorithm and artificial **neural network**

AU Brusic V (Reprint); Rudy G; Honeyman M; Hammer J; Harrison L

SO BIOINFORMATICS, (JUN 1998) Vol. 14, No. 2, pp. 121-130.

Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.

ISSN: 1367-4803.

AB Motivation: Prediction methods for identifying **binding** peptides could minimize the number of peptides required to be synthesized and assayed, and thereby facilitate the identification of potential

T-cell

epitopes. We developed a bioinformatic method for the prediction of **peptide binding** to MHC class II molecules.

Results: Experimental **binding** data and expert knowledge of anchor positions and **binding** motifs were combined with an evolutionary algorithm (EA) and an artificial **neural network** (ANN): **binding** data extraction -->

peptide alignment --> ANN training and classification. This method, termed PERUN, was implemented for the prediction of peptides that bind to HLA-DR4(B1*0401). The respective positive predictive values of PERUN predictions of high-, moderate-, low- and zero-affinity binder-a were assessed as 0.8, 0.7, 0.5 and 0.8 by cross-validation, and 1.0, 0.8, 0.3 and 0.7 by experimental **binding**. This illustrates the synergy between experimentation and computer modeling, and its

application

to the identification of potential immunotherapeutic peptides.

L3 ANSWER 8 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Capping and dynamic relation between domains 1 and 2 of gelsolin

AU Feinberg J; Kwiatek O; Astier C; Diennet S; Mery J; Heitz F; Benyamin Y; Roustan C (Reprint)

SO JOURNAL OF PEPTIDE SCIENCE, (APR 1998) Vol. 4, No. 2, pp. 116-127.

Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX, ENGLAND PO19 1UD.

ISSN: 1075-2617.

AB Gelsolin is a protein that severs and caps actin filaments. The two activities are located in the N-terminal half of the gelsolin molecules. Severing and subsequent capping requires the **binding** of domains 2 and 3 (S2-3) to the side of the filaments to position the N-terminal domain 1 (S1) at the barbed end of actin (actin subdomains 1 and 3). The results provide a structural basis for the gelsolin capping mechanism.

The

effects of a synthetic **peptide** derived from the sequence of a **binding** site located in gelsolin S2 on actin properties have been studied, CD and IR spectra indicate that this **peptide** presented

a secondary structure in solution which would be similar to that expected for the native 1 length gelsolin molecule. The **binding** of the synthetic **peptide** induces conformational changes in actin subdomain 1 and actin oligomerization. An increase in the polymerization rate was observed, which could be attributed to a nucleation kinetics effect. The combined effects of two gelsolin fragments, the synthetic **peptide** derived from an S2 sequence and the purified segment 1 (S1), were also investigated as a molecule model. The two fragments induced nucleation enhancement and inhibited actin depolymerization, two characteristic properties of capping. In conclusion, for the first time

it

is reported that the **binding** of a small synthetic fragment is sufficient to promote efficient capping by S1 at the barbed end of actin filaments. (C) 1998 European **Peptide** Society and John Wiley & Sons, Ltd.

L3 ANSWER 9 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Strategies for identifying and predicting islet autoantigen T-cell epitopes in insulin-dependent diabetes mellitus

AU Honeyman M C (Reprint); Brusic V; Harrison L C

SO ANNALS OF MEDICINE, (OCT 1997) Vol. 29, No. 5, pp. 401-404.

Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 ONE.

ISSN: 0785-3890.

AB T cells recognize **peptide** epitopes bound to major histocompatibility complex molecules. Human T-cell epitopes have diagnostic and therapeutic applications in autoimmune diseases. However, their accurate definition within an autoantigen by T-cell bioassay, usually proliferation, involves many costly peptides and a large amount

of

blood, We have therefore developed a strategy to predict T-cell epitopes and applied it to tyrosine phosphatase IA-2, an autoantigen in IDDM, and HLA-DR4(*0401). First, the **binding** of synthetic overlapping peptides encompassing IA-2 was measured directly to purified DR4. Secondly, a large amount of HLA-DR4 **binding** data were analysed by alignment using a genetic algorithm and were used to train an artificial **neural network** to predict the affinity of **binding**. This bioinformatic prediction method was then validated experimentally and used to predict DR4 **binding** peptides in IA-2. The **binding** set encompassed 85% of experimentally determined T-cell epitopes. Both the experimental and bioinformatic methods had high negative predictive values, 92% and 95%, indicating that this strategy of combining experimental results with computer modelling should lead to a significant reduction in the amount of blood and the number of peptides required to define T-cell epitopes in humans.

L3 ANSWER 10 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)

TI Generation and phenotypic characterization of new human ovarian cancer cell lines with the identification of antigens potentially recognizable

by

HLA-restricted cytotoxic T cells

AU Ramakrishna V; Negri D R M; Brusic V; Fontanelli R; Canevari S; Bolis G; Castelli C; Parmiani G (Reprint)

SO INTERNATIONAL JOURNAL OF CANCER, (26 SEP 1997) Vol. 73, No. 1, pp. 143-150.

Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.

ISSN: 0020-7136.

AB This study describes a simple method for long-term establishment of human ovarian tumor lines and prediction of T-cell epitopes that could be potentially useful in the generation of tumor-specific cytotoxic T lymphocytes (CTLs). Nine ovarian tumor lines (INT.Ov) were generated from

solid primary or metastatic tumors as well as from ascitic fluid, Notably all lines expressed HLA class I, intercellular adhesion molecule-1 (ICAM-1), polymorphic epithelial mucin (PEM) and cytokeratin (CK), but not HLA class II, B7.1 (CD80) or BAGE, While of the 9 lines tested 4 (INT.Ov1, 2, 5 and 6) expressed the folate receptor (FR-alpha) and 6 (INT.Ov1, 2, 5, 6, 7 and 9) expressed the epidermal growth factor receptor (EGFR); MAGE-1 and p185(HER-2/neu) were only found in 2 lines (INT.Ov1 and 2) and GAGE-1 expression in 1 line (INT.Ov2). The identification of class I MHC ligands and T-cell epitopes within protein antigens was achieved by applying several theoretical methods including: 1) similarity or homology searches to MHCPEP; 2) BIMAS and 3) artificial **neural network**-based predictions of proteins MACE, GAGE, EGFR, p185(HER-2/neu) and FR-alpha expressed in INT.Ov lines, Because of the high frequency of expression of some of these proteins in ovarian cancer and the ability to determine HLA **binding** peptides efficiently, it is expected that after appropriate screening, a large cohort of ovarian cancer patients may become candidates to receive **peptide** based vaccines. (C) 1997 Wiley-Liss, Inc.

L3 ANSWER 11 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI Two complementary methods for predicting peptides **binding** major histocompatibility complex molecules
 AU Gulukota K (Reprint); Sidney J; Sette A; DeLisi C
 SO JOURNAL OF MOLECULAR BIOLOGY, (18 APR 1997) Vol. 267, No. 5, pp. 1258-1267.
 Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON, ENGLAND NW1 7DX. ISSN: 0022-2836.
 AB Peptides that bind to major histocompatibility complex products (MHC) are known to exhibit certain sequence motifs which, though common, are neither necessary nor sufficient for **binding**: MHCs bind certain peptides that do not have the characteristic motifs and only about 30% of the peptides having the required motif, bind. In order to develop and test more accurate methods we measured the **binding** affinity of 463 nonamer peptides to HLA-A2.1. We describe two methods for predicting whether a given **peptide** will bind to an MHC and apply them to these peptides. One method is based on simulating a **neural network** and another, called the polynomial method, is based on statistical parameter estimation assuming independent **binding** of the side-chains of residues. We compare these methods with each other and with standard motif-based methods. The two methods are complementary, and both are superior to sequence motifs. The **neural net** is superior to simple motif searches in eliminating false positives. Its behavior can be coarsely tuned to the strength of **binding** desired and it is extendable in a straightforward fashion to other alleles. The polynomial method, on the other hand, has high sensitivity and is a superior method for eliminating false negatives. We discuss the validity of the independent **binding** assumption in such predictions. (C) 1997 Academic Press Limited.

L3 ANSWER 12 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI MYOMODULIN GENE OF LYMNAEA - STRUCTURE, EXPRESSION, AND ANALYSIS OF NEUROPEPTIDES
 AU KELLETT E; PERRY S J (Reprint); SANTAMA N; WORSTER B M; BENJAMIN P R; BURKE J F
 SO JOURNAL OF NEUROSCIENCE, (15 AUG 1996) Vol. 16, No. 16, pp. 4949-4957. ISSN: 0270-6474.
 AB The myomodulin family of neuropeptides is an important group of neural cotransmitters in molluscs and is known to be present in the

neural network that controls feeding behavior in the snail *Lymnaea*. We show that a single gene encodes five structurally similar forms of myomodulin: GLQMLRLamide, QIPMLRLamide, SMSMLRLamide, SLTMLRLamide, and PMSMLRLamide, the latter being present in nine copies. Analysis of the organization of the gene indicates that it is transcribed as a single spliced transcript from an upstream promoter region that contains multiple cAMP-responsive elements, as well as putative elements with homology to tissue-specific promoter-binding sites. The presence in nervous tissue of two of the peptides, GLQMLRLamide and PMSMLRLamide, is confirmed by mass spectrometry. In situ hybridization analysis indicates that the gene is expressed in specific cells in all ganglia of the CNS of *Lymnaea*, which will allow physiological analysis of the function of myomodulins at the level of single identified neurons.

L3 ANSWER 13 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI PREDICTION OF **BINDING** TO MHC CLASS-I MOLECULES
 AU ADAMS H P (Reprint); KOZIOL J A
 SO JOURNAL OF IMMUNOLOGICAL METHODS, (25 SEP 1995) Vol. 185, No. 2, pp. 181-190.
 ISSN: 0022-1759.

AB The **binding** of antigenic **peptide** sequences to major histocompatibility complex (MHC) molecules is a prerequisite for stimulation of cytotoxic T cell responses. **Neural networks** are here used to predict the **binding** capacity of polypeptides to MHC class I molecules encoded by the gene HLA-A* 0201. Given a large database of 552 nonamers and 486 decamers and their known **binding** capacities, the **neural networks** achieve a predictive hit rate of 0.78 for classifying peptides which

might induce an immune response (good or intermediate binders) vs. those which cannot (weak or non-binders). The **neural nets** also depict specific motifs for different **binding** capacities. This approach is in principle applicable to all MHC class I and II molecules, given a suitable set of known **binding** capacities. The trained networks can then be used to perform a systematic search through all pathogen or tumor antigen protein sequences for potential cytotoxic T lymphocyte epitopes.

L3 ANSWER 14 OF 14 SCISEARCH COPYRIGHT 1999 ISI (R)
 TI ATRIAL-NATRIURETIC-**PEPTIDE** INHIBITS THE SPONTANEOUS CONTRACTIONS OF RABBIT ISOLATED ILEUM
 AU BLANDIZZI C; AGEN C; NATALE G; DELTACCA M (Reprint)
 SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (JUL 1992) Vol. 44, No. 7, pp. 615-617.
 ISSN: 0022-3573.

AB The present study investigates the effects of atriopeptin II on spontaneous phasic contractions of rabbit isolated ileum. Atriopeptin II caused a significant and concentration-dependent decrease in ileum motor activity. This effect was mimicked by 8-Br-cGMP and it was not affected by pretreatment with tetrodotoxin. Verapamil significantly decreased ileum contractions; however, in the presence of this calcium blocker, atriopeptin II further reduced ileal motility. These findings demonstrate that atriopeptin II depresses the motility of rabbit ileum through a cGMP-dependent mechanism and suggest that neither ileal **neural networks** nor extracellular calcium are involved in this effect.

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=> S PEPTIDE AND BINDING AND NEURAL NET?

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90532 NEURAL
91004 NET?
3924 NEURAL NET?
(NEURAL(W)NET?)

L4 13 PEPTIDE AND BINDING AND NEURAL NET?

=> D TI AU SO AB 1-13

L4 ANSWER 1 OF 13 MEDLINE

TI Application of an artificial **neural network** to predict specific class I MHC **binding peptide** sequences [see comments].

AU Milik M; Sauer D; Brunmark A P; Yuan L; Vitiello A; Jackson M R; Peterson P A; Skolnick J; Glass C A

SO NATURE BIOTECHNOLOGY, (1998 Aug) 16 (8) 753-6.
Journal code: CQ3. ISSN: 1087-0156.

AB Computational methods were used to predict the sequences of peptides that bind to the MHC class I molecule, K(b). The rules for predicting **binding** sequences, which are limited, are based on preferences for certain amino acids in certain positions of the **peptide**. It is apparent though, that **binding** can be influenced by the amino acids in all of the positions of the **peptide**. An artificial **neural network** (ANN) has the ability to simultaneously analyze the influence of all of the amino acids of the **peptide** and thus may improve **binding** predictions. ANNs were compared to statistically analyzed peptides for their abilities to predict the sequences of K(b) **binding** peptides. ANN systems were trained on a library of **binding** and nonbinding **peptide** sequences from a phage display library. Statistical and ANN methods identified strong **binding** peptides with preferred amino acids. ANNs detected more subtle **binding** preferences, enabling them to predict medium **binding** peptides. The ability to predict class I MHC molecule **binding** peptides is useful for immunological therapies involving cytotoxic-T cells.

L4 ANSWER 2 OF 13 MEDLINE

TI Relationship between **peptide** selectivities of human transporters associated with antigen processing and HLA class I molecules.

AU Daniel S; Brusica V; Caillat-Zucman S; Petrovsky N; Harrison L; Riganelli D; Sinigaglia F; Gallazzi F; Hammer J; van Endert P M

SO JOURNAL OF IMMUNOLOGY, (1998 Jul 15) 161 (2) 617-24.
Journal code: IFB. ISSN: 0022-1767.

AB Efficiency of presentation of a **peptide** epitope by a MHC class I molecule depends on two parameters: its **binding** to the MHC molecule and its generation by intracellular Ag processing. In contrast to the former parameter, the mechanisms underlying **peptide** selection in Ag processing are poorly understood. **Peptide**

translocation by the TAP transporter is required for presentation of most epitopes and may modulate **peptide** supply to MHC class I molecules. To study the role of human TAP for **peptide** presentation by individual HLA class I molecules, we generated artificial **neural networks** capable of predicting the affinity of TAP for random sequence 9-mer peptides. Using **neural network**-based predictions of TAP affinity, we found that peptides eluted from three different HLA class I molecules had higher TAP affinities than control peptides with equal **binding** affinities for the same HLA class I molecules, suggesting that human TAP may contribute to epitope selection. In simulated TAP **binding** experiments with 408 HLA class I **binding** peptides, HLA class I molecules differed significantly with respect to TAP affinities of their ligands. As a result, some class I molecules, especially HLA-B27, may be particularly efficient in presentation of cytosolic peptides with low concentrations, while most class I molecules may predominantly present abundant cytosolic peptides.

L4 ANSWER 3 OF 13 MEDLINE

TI Prediction of MHC class II-**binding** peptides using an evolutionary algorithm and artificial **neural network**.

AU Brusic V; Honeyman G; Hammer J; Harrison L

SO BIOINFORMATICS, (1998) 14 (2) 121-30.

Journal code: CW9. ISSN: 1367-4803.

AB MOTIVATION: Prediction methods for identifying **binding** peptides could minimize the number of peptides required to be synthesized and assayed, and thereby facilitate the identification of potential T-cell epitopes. We developed a bioinformatic method for the prediction of **peptide binding** to MHC class II molecules. RESULTS: Experimental **binding** data and expert knowledge of anchor positions and **binding** motifs were combined with an evolutionary algorithm (EA) and an artificial **neural network** (ANN): **binding** data extraction --> **peptide** alignment --> ANN training and classification. This method, termed PERUN, was implemented for the prediction of peptides that bind to HLA-DR4(B1*0401). The respective positive predictive values of PERUN predictions of high-, moderate-, low- and zero-affinity binders were assessed as 0.8, 0.7, 0.5 and 0.8 by cross-validation, and 1.0, 0.8, 0.3 and 0.7 by experimental **binding**. This illustrates the synergy between experimentation and computer modeling, and its application to the identification of potential immunotherapeutic peptides. AVAILABILITY: Software and data are available from the authors upon request. CONTACT: vladimir@wehi.edu. au

L4 ANSWER 4 OF 13 MEDLINE

TI Hair cycle-dependent expression of corticotropin-releasing factor (CRF) and CRF receptors in murine skin.

AU Roloff B; Fechner K; Slominski A; Furkert J; Botchkarev V A; Bulfone-Paus S; Zipper J; Krause E; Paus R

SO FASEB JOURNAL, (1998 Mar) 12 (3) 287-97.

Journal code: FAS. ISSN: 0892-6638.

AB We demonstrate the presence and hair cycle-dependent expression of corticotropin-releasing factor (CRF) and CRF receptors (CRF-R) in C57BL/6 mouse skin. To correlate this with a physiological, developmentally controlled tissue remodeling process, we have analyzed CRF and CRF-R expression during defined stages of the murine hair cycle with its rhythmic changes between growth (anagen), regression (catagen), and resting (telogen). Using reversed-phase HPLC combined with two

independent

anti-CRF radioimmunoassays, we have identified CRF in murine skin.

Maximal

CRF levels were found in anagen III-IV skin, and minimal values were detected in catagen and telogen skin. By immunofluorescence, maximal CRF immunoreactivity (CRF-IR) was seen in the basal epidermis, nerve bundles

of skin, the outer root sheath and matrix region of anagen IV-VI follicles, and defined sections of their pericellular **neural network**, whereas catagen and telogen skin displayed minimal CRF-IR. Using quantitative autoradiography and ¹²⁵I-CRF as a tracer, high-affinity **binding** sites for CRF were detected in murine skin. The highest density of specific **binding** sites was detected in the panniculus carnosus, the epidermis, and the hair follicle. CRF-R type 1 (CRF-R1) IR was detected by immunohistology mainly in the outer root sheath, hair matrix, and dermal papilla of anagen VI follicles, as well as in the inner and outer root sheaths of early catagen follicles. CRF-R1 expression was also hair cycle dependent. Therefore, in normal murine skin, the CRF-CRF-R signaling system may operate as an additional neuroendocrine pathway regulating skin functions, possibly in the context of cutaneous stress responses.

L4 ANSWER 5 OF 13 MEDLINE

TI HIV type 1 V3 serotyping of Tanzanian samples: probable reasons for mismatching with genetic subtyping.

AU Hoelscher M; Hanker S; Barin F; Cheingsong-Popov R; Dietrich U; Jordan-Harder B; Olaleye D; Nagele E; Markuzzi A; Mwakagile D; Minja F; Weber J; Gurtler L; Von Sonnenburg F

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1998 Jan 20) 14 (2) 139-49. Journal code: ART. ISSN: 0889-2229.

AB HIV-1 V3 serotyping is used to classify immunodeficiency viruses on the basis of antibody **binding** to V3 peptides derived from env genetic subtypes. Although it shows a reasonable overlap, it has been reported to be distinct from viral genetic subtypes. The aim of this

study is to determine the feasibility of HIV-1 serotyping to predict genetic subtypes in an East African setting, where multiple HIV-1 subtypes have coexisted for many years. HIV-1 genetic subtypes of 86 AIDS patients in Mbeya Town, southwest Tanzania, were determined, using env nucleic acid sequencing as the basis for comparison. Those data were compared with V3 serotyping results obtained by four different methodologies. Four HIV-1 genetic subtypes were identified, including A (25, 29%), C (47, 55%), D (13, 15%), and G (1, 1%). The sensitivity and specificity of those serotyping assays varied considerably: sensitivity for genetic subtype A (40-48%), C (52-96%), and D (9-31%); and specificity for genetic subtype

A (77-95%), C (46-63%), and D (97-100%). We further tried to identify reasons for the discrepancies between serotyping results and genetic subtypes. By means of logistic regression analysis three amino acid residues within the V3 loop (positions 12, 13, and 19; V, H, and A for serotype A, I, R, and T for serotype C) were found to be most important for antibody **binding**; a deviation from the subtype-specific amino acids was highly related to mismatched results. In addition, we

have shown that phenetic analysis of V3 amino acid sequence data could be used to predict the majority of V3 serotypes (93-94%). Our data demonstrated that for the majority of specimens HIV-1 V3 serotyping results closely match the subtype of the analyzed sample as revealed by the V3 loop amino acid sequence. However, our data demonstrate that HIV-1 serotyping is not sufficiently accurate to predict genetic subtypes in Tanzania, where subtypes A, C, D, and G are circulating. This was due to highly similar amino acid sequences throughout the prevalent genetic subtypes, which caused the inability of HIV-1 V3 serotyping to differentiate subtype A from C as well as D from C. Instead, the serotyping results reflect the frequency distribution of V3 serotypes. To investigate HIV-1 genetic subtypes in population-based studies in this African setting additional

or modified algorithms are needed.

L4 ANSWER 6 OF 13 MEDLINE

TI Strategies for identifying and predicting islet autoantigen T-cell epitopes in insulin-dependent diabetes mellitus.

AU Honeyman M C; Brusic V; Harrison L C

SO ANNALS OF MEDICINE, (1997 Oct) 29 (5) 401-4.
Journal code: AMD. ISSN: 0785-3890.

AB T cells recognize **peptide** epitopes bound to major histocompatibility complex molecules. Human T-cell epitopes have diagnostic and therapeutic applications in autoimmune diseases. However, their accurate definition within an autoantigen by T-cell bioassay, usually proliferation, involves many costly peptides and a large amount of blood. We have therefore developed a strategy to predict T-cell epitopes and applied it to tyrosine phosphatase IA-2, an autoantigen in IDDM, and HLA-DR4(*0401). First, the **binding** of synthetic overlapping peptides encompassing IA-2 was measured directly to purified DR4. Secondly, a large amount of HLA-DR4 **binding** data were analysed by alignment using a genetic algorithm and were used to train an artificial **neural network** to predict the affinity of **binding**. This bioinformatic prediction method was then validated experimentally and used to predict DR4 **binding** peptides in IA-2. The **binding** set encompassed 85% of experimentally determined T-cell epitopes. Both the experimental and bioinformatic methods had high negative predictive values, 92% and 95%, indicating that this strategy of combining experimental results with computer modelling should lead to a significant reduction in the amount of blood and the number of peptides required to define T-cell epitopes in humans.

L4 ANSWER 7 OF 13 MEDLINE

TI Generation and phenotypic characterization of new human ovarian cancer cell lines with the identification of antigens potentially recognizable by

HLA-restricted cytotoxic T cells.

AU Ramakrishna V; Negri D R; Brusic V; Fontanelli R; Canevari S; Bolis G; Castelli C; Parmiani G

SO INTERNATIONAL JOURNAL OF CANCER, (1997 Sep 26) 73 (1) 143-50.
Journal code: GQU. ISSN: 0020-7136.

AB This study describes a simple method for long-term establishment of human ovarian tumor lines and prediction of T-cell epitopes that could be potentially useful in the generation of tumor-specific cytotoxic T lymphocytes (CTLs). Nine ovarian tumor lines (INT.Ov) were generated from solid primary or metastatic tumors as well as from ascitic fluid. Notably all lines expressed HLA class I, intercellular adhesion molecule-1 (ICAM-1), polymorphic epithelial mucin (PEM) and cytokeratin (CK), but

not

HLA class II, B7.1 (CD80) or BAGE. While of the 9 lines tested 4

(INT.Ov1,

2, 5 and 6) expressed the folate receptor (FR-alpha) and 6 (INT.Ov1, 2,

5,

6, 7 and 9) expressed the epidermal growth factor receptor (EGFR); MAGE-1 and p185HER-2/neu were only found in 2 lines (INT.Ov1 and 2) and GAGE-1 expression in 1 line (INT.Ov2). The identification of class I MHC ligands and T-cell epitopes within protein antigens was achieved by applying several theoretical methods including: 1) similarity or homology searches to MHCPEP; 2) BIMAS and 3) artificial **neural network**-based predictions of proteins MAGE, GAGE, EGFR, p185HER-2/neu and FR-alpha expressed in INT.Ov lines. Because of the high frequency of expression of some of these proteins in ovarian cancer and the ability to determine HLA **binding** peptides efficiently, it is expected that after appropriate screening, a large cohort of ovarian cancer patients

may

become candidates to receive **peptide**-based vaccines.

L4 ANSWER 8 OF 13 MEDLINE

TI **Neural network** prediction of translation initiation sites in eukaryotes: perspectives for EST and genome analysis.

AU Pedersen A G; Nielsen H

SO ISMB, (1997) 5 226-33.
Journal code: CCP.

AB Translation in eukaryotes does not always start at the first AUG in an mRNA, implying that context information also plays a role. This makes prediction of translation initiation sites a non-trivial task, especially when analysing EST and genome data where the entire mature mRNA sequence is not known. In this paper, we employ artificial **neural networks** to predict which AUG triplet in an mRNA sequence is the start codon. The trained networks correctly classified 88% of Arabidopsis and 85% of vertebrate AUG triplets. We find that our trained **neural networks** use a combination of local start codon context and global sequence information. Furthermore, analysis of false predictions shows that AUGs in frame with the actual start codon are more frequently selected than out-of-frame AUGs, suggesting that our networks use reading frame detection. A number of conflicts between **neural network** predictions and database annotations are analysed in detail, leading to identification of possible database errors.

L4 ANSWER 9 OF 13 MEDLINE

TI Two complementary methods for predicting peptides **binding** major histocompatibility complex molecules.

AU Gulukota K; Sidney J; Sette A; DeLisi C

SO JOURNAL OF MOLECULAR BIOLOGY, (1997 Apr 18) 267 (5) 1258-67.
Journal code: J6V. ISSN: 0022-2836.

AB Peptides that bind to major histocompatibility complex products (MHC) are known to exhibit certain sequence motifs which, though common, are neither necessary nor sufficient for **binding**: MHCs bind certain peptides that do not have the characteristic motifs and only about 30% of the peptides having the required motif, bind. In order to develop and test more accurate methods we measured the **binding** affinity of 463 nonamer peptides to HLA-A2.1. We describe two methods for predicting whether a given **peptide** will bind to an MHC and apply them to these peptides. One method is based on simulating a **neural network** and another, called the polynomial method, is based on statistical parameter estimation assuming independent **binding** of the side-chains of residues. We compare these methods with each other and with standard motif-based methods. The two methods are complementary, and both are superior to sequence motifs. The **neural net** is superior to simple motif searches in eliminating false positives. Its behavior can be coarsely tuned to the strength of **binding** desired and it is extendable in a straightforward fashion to other alleles. The polynomial method, on the other hand, has high sensitivity and is a superior method for eliminating false negatives. We discuss the validity of the independent **binding** assumption in such predictions.

L4 ANSWER 10 OF 13 MEDLINE

TI Experimentally determined weight matrix definitions of the initiator and TBP **binding** site elements of promoters.

AU Kraus R J; Murray E E; Wiley S R; Zink N M; Loritz K; Gelembiuk G W; Mertz J E

SO NUCLEIC ACIDS RESEARCH, (1996 Apr 15) 24 (8) 1531-9.
Journal code: O8L. ISSN: 0305-1048.

AB The basal elements of class II promoters are: (i) a -30 region, recognized by TATA **binding** protein (TBP); (ii) an initiator (Inr) surrounding the start site for transcription; (iii) frequently a downstream (+10 to +35) element. To determine the sequences that specify an Inr, we performed a saturation mutagenesis of the Inr of the SV40 major

late promoter (SV40-MLP). The transcriptional activity of each mutant was determined both *in vivo* and *in vitro*. An excellent correlation between transcriptional activity and closeness of fit to the optimal Inr sequence,

5'-CAG/TT-3', was found to exist both *in vivo* and *in vitro*. Employing a **neural network** technique we generated from these data a weight matrix definition of an Inr that can be used to predict the activity of a given sequence as an Inr. Using saturation mutagenesis data of TBP **binding** sites we likewise generated a weight matrix definition of the -30 region element. We conclude the following: (i) Inrs are defined by the nucleotides immediately surrounding the transcriptional

start site; (ii) most, if not all, Inrs are recognized by the same general

transcription factor(s). We propose that the mechanism of transcription initiation is fundamentally conserved, with the formation of pre-initiation complexes involving the concurrent **binding** of general transcription factors to the -30, Inr and, possibly, downstream elements of class II promoters.

L4 ANSWER 11 OF 13 MEDLINE

TI Prediction of **binding** to MHC class I molecules.

AU Adams H P; Koziol J A

SO JOURNAL OF IMMUNOLOGICAL METHODS, (1995 Sep 25) 185 (2) 181-90.
Journal code: IFE. ISSN: 0022-1759.

AB The **binding** of antigenic **peptide** sequences to major histocompatibility complex (MHC) molecules is a prerequisite for stimulation of cytotoxic T cell responses. **Neural networks** are here used to predict the **binding** capacity of polypeptides to MHC class I molecules encoded by the gene HLA-A*0201. Given a large database of 552 nonamers and 486 decamers and their known **binding** capacities, the **neural networks** achieve a predictive hit rate of 0.78 for classifying peptides which

might

induce an immune response (good or intermediate binders) vs. those which cannot (weak or non-binders). The **neural nets** also depict specific motifs for different **binding** capacities. This approach is in principle applicable to all MHC class I and II molecules, given a suitable set of known **binding** capacities. The trained networks can then be used to perform a systematic search through all pathogen or tumor antigen protein sequences for potential cytotoxic T lymphocyte epitopes.

L4 ANSWER 12 OF 13 MEDLINE

TI The rational design of amino acid sequences by artificial **neural networks** and simulated molecular evolution: de novo design of an idealized leader peptidase cleavage site [see comments].

AU Schneider G; Wrede P

SO BIOPHYSICAL JOURNAL, (1994 Feb) 66 (2 Pt 1) 335-44.
Journal code: A5S. ISSN: 0006-3495.

AB A method for the rational design of locally encoded amino acid sequence features using artificial **neural networks** and a technique for simulating molecular evolution has been developed. De novo in machine design of Escherichia coli leader peptidase (SP1) cleavage sites serves as an example application. A modular **neural network** system that employs sequence descriptions in terms of physicochemical properties has been trained on the recognition of characteristic cleavage site features. It is used for sequence qualification in the design cycle, representing the sequence fitness function. Starting from a random sequence several cleavage site sequences were generated by a simulated molecular evolution technique. It is based on a simple genetic algorithm that takes the quality values calculated by the artificial **neural network** as a heuristic for

inductive sequence optimization. Simulated in vivo mutation and selection allows the identification of predominant sequence positions in Escherichia coli signal **peptide** cleavage site regions (positions -2 and -6). Various amino acid distance maps are used to define metrics for the step size of mutations. Position-specific mutability values indicate sequence positions exposed to high or low selection pressure in the simulations. The use of several distance maps leads to different courses of optimization and to various idealized sequences. It is concluded that amino acid distances are context dependent. Furthermore, a method for identification of local optima during sequence optimization is presented.

L4 ANSWER 13 OF 13 MEDLINE

TI Using a **neural network** to identify potential HLA-DR1 **binding** sites within proteins.

AU Bisset L R; Fierz W

SO JOURNAL OF MOLECULAR RECOGNITION, (1993 Mar) 6 (1) 41-8.

Journal code: A00. ISSN: 0952-3499.

AB The presentation by antigen-presenting cells of immunodominant **peptide** segments in association with major histocompatibility complex (MHC) encoded proteins is fundamental to the efficacy of a specific immune response. One approach used to identify immunodominant segments within proteins has involved the development of predictive algorithms which utilize amino acid sequence data to identify structural characteristics or motifs associated with in vivo antigenicity. The parallel-computing technique termed '**neural networking**' has recently been shown to be remarkably efficient at addressing the problem of pattern recognition and can be applied to predict protein secondary structure attributes directly from amino acid sequence data. In order to examine the potential of a **neural network** to generalize **peptide** structural features related to **binding** within class II MHC-encoded proteins, we have trained a **neural network** to determine whether or not any given amino acid of a protein is part of a **peptide** segment capable of **binding** to HLA-DR1. We report that a **neural network** trained on a data base consisting of **peptide** segments known to bind to HLA-DR1 is able to generalize features relating to HLA-DR1-**binding** capacity ($r = 0.17$ and $p = 0.0001$).

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TI An object-oriented environment for artificial evolution of protein sequences: the example of rational design of transmembrane sequences.

AU Milik, M.; Skolnick, J. (Scripps Res. Instn., La Jolla, CA, USA)

SO Evolutionary Programming IV. Proceedings of the Fourth Annual Conference on Evolutionary Programming

Editor(s): McDonnell, J.R.; Reynolds, R.G.; Fogel, D.B.

Cambridge, MA, USA: MIT Press, 1995. p.603-13 of xx+805 pp. 3 refs.

Conference: San Diego, CA, USA, 1-3 March 1995

ISBN: 0-262-13317-2

AB A system is presented for generating ***peptide*** sequences with desirable properties using a combination of ***neural*** ***network*** and artificial evolution. The process is illustrated by an example of a practical problem of generating artificial transbilayer peptides. The peptides generated in the process of artificial evolution have the physico-chemical properties of transmembrane peptides, and form stable transmembrane structures in testing Monte Carlo simulations. The artificial evolution system is designed to emulate natural evolution; therefore it is of both practical and theoretical interest, both in terms of rational design of protein sequences and modeling of natural evolution of proteins.

TI Development of simple fitness landscapes for peptides by artificial neural filter systems.

AU Schneider, G.; Schuchhardt, J.; Wrede, P. (Freie Univ. Berlin, Germany)

SO Biological Cybernetics (Aug. 1995) vol.73, no.3, p.245-54. 61 refs.

CODEN: BICYAF ISSN: 0340-1200

AB The applicability of artificial neural filter systems as fitness functions for sequence-oriented ***peptide*** design was evaluated. Two example applications were selected: classification of dipeptides according to their hydrophobicity and classification of proteolytic cleavage-sites of protein precursor sequences according to their mean hydrophobicities and mean side-chain volumes. The cleavage-sites covered 12 residues. In the dipeptide experiments the objective was to separate a selected set of molecules from all other possible dipeptide sequences. Perceptrons, feedforward networks with one hidden layer, and a hybrid network were applied. The filters were trained by a (1, lambda) evolution strategy. Two types of network units employing either a sigmoidal or a unimodal transfer function were used in the feedforward filters, and their influence on classification was investigated. The two-layer hybrid network employed gaussian activation functions. To analyze classification of the different filter systems, their output was plotted in the two-dimensional sequence space. The diagrams were interpreted as fitness landscapes qualifying the markedness of a characteristic ***peptide*** feature which can be used as a guide through sequence space for rational ***peptide*** design. It is demonstrated that the applicability of neural filter systems as a heuristic method for sequence optimization depends on both the appropriate network architecture and selection of

representative sequence data. The networks with unimodal activation functions and the hybrid networks both led to a number of local optima. However, the hybrid networks produced the best prediction results. In contrast, the filters with sigmoidal activation produced good reclassification results leading to fitness landscapes lacking unreasonable local optima. Similar results were obtained for classification of both dipeptides and cleavage-site sequences.

TI The rational design of amino acid sequences by artificial ***neural***
networks and simulated molecular evolution: de novo design of an
idealized leader peptidase cleavage site.

AU Schneider, G.; Wrede, P. (Inst. fur Experimentalphysik, Freie Univ.,
Berlin, Germany)

SO Biophysical Journal (Feb. 1994) vol.66, no.2, pt.1, p.335-44. 30 refs.

Price: CCCC 0006-3495/94/02/335/10\$2.00

CODEN: BIOJAU ISSN: 0006-3495

AB A method for the rational design of locally encoded amino acid sequence features using artificial ***neural*** ***networks*** and a technique for simulating molecular evolution has been developed. De novo in machine design of Escherichia coli leader peptidase (SP1) cleavage sites serves as an example application. A modular ***neural*** ***network*** system that employs sequence descriptions in terms of physicochemical properties has been trained on the recognition of characteristic cleavage site features. It is used for sequence qualification in the design cycle, representing the sequence fitness function. Starting from a random sequence several cleavage site sequences were generated by a simulated molecular evolution technique. It is based on a simple genetic algorithm that takes the quality values calculated by the artificial ***neural*** ***network*** as a heuristic for inductive sequence optimization. Simulated in vivo mutation and selection allows the identification of predominant sequence positions in Escherichia coli signal ***peptide*** cleavage site regions (positions -2 and -6). Various amino acid distance maps are used to define metrics for the step size of mutations. Position-specific mutability values indicate sequence positions exposed to high or low selection pressure in the simulations. The use of several distance maps leads to different courses of optimization and to various idealized sequences. It is concluded that amino acid distances are context dependent. Furthermore, a method for identification of local optima during sequence optimization is presented.

L2 ANSWER 11 OF 12 INSPEC COPYRIGHT 1999 IEE

TI Peptides secondary structure prediction with ***neural***
networks : a criterion for building appropriate learning sets.

AU Ruggiero, C.; Sacile, R. (Dept. of Commun., Comput. and Syst. Sci., Genoa Univ., Italy); Rauch, G.

SO IEEE Transactions on Biomedical Engineering (Nov. 1993) vol.40, no.11,
p.1114-21. 24 refs.

Price: CCCC 0018-9294/93/\$03.00

CODEN: IEBEAX ISSN: 0018-9294

AB Artificial ***neural*** ***networks*** have been recently applied with success for protein secondary structure prediction. So far, one of the two main aspects on which ***neural*** ***net*** performance

depends, the topology of the net, has been considered. The present work addresses the other main aspect, the building up of the learning set. The author presents a criterion to build up suitable learning sets based on the alpha-helix percentage. Starting from a set of several well known proteins, the author formed 7 groups of proteins with similar helix percentages and used them for the learning of the same ***neural*** ***net***. The author found that the best secondary structure prediction for each of the tested proteins (not belonging to the initial set) was the one obtained using the learning set whose helix percentage was closest to that of the tested protein. The accuracy of correct prediction of the author's method on 3 types of secondary structure (alpha-helix, beta-sheet and coil), has been compared with the accuracy of other secondary structure prediction methods.